

ARTICLE 34

1. A fusion protein comprising a soluble protein joined without an intervening peptide linker to an immunoglobulin (Ig) domain, wherein the soluble protein is selected from the group consisting of a growth factor, a cytokine that is not IL-10, and an active variant thereof, and wherein the immunoglobulin domain does not contain a variable region.

2. A fusion protein comprising a soluble protein joined at its carboxy-terminus to the amino terminus of an immunoglobulin domain, wherein the soluble protein is selected from the group consisting of a growth factor, a cytokine that is not interleukin-10 (IL-10) or an interferon, and an active variant thereof, wherein the immunoglobulin domain does not contain a variable region, and wherein the soluble protein and the immunoglobulin domain are joined by a peptide linker that is not AspProGlu or Ser.

3. The fusion protein of claim 2, wherein the peptide linker is SerGly.

~~4. The fusion protein of claim 2, wherein the peptide linker is Ser(GlyGlySer)_n, wherein n is 1 to 7.~~

5. The fusion protein of claim 2, wherein the peptide linker is Ser(GlyGlySer) or Ser(GlyGlySer)₂.

6. The fusion protein of any one of claims 1-5, wherein the Ig domain is selected from the group consisting of IgG-Fc, IgG-C_H and IgG-C_L.

7. The fusion protein of any one of Claims 1-5, wherein the soluble protein is a member of the growth hormone (GH) supergene family.

~~8. The fusion protein of any one of Claims 1-5, wherein the soluble protein is granulocyte-colony stimulating factor (G-CSF).~~

9. The fusion protein of claim 8, wherein the fusion protein has an EC₅₀ of less than about 300 ng/ml in a G-CSF-dependent cell assay.

10. The fusion protein of claim 8, wherein serine is substituted for cysteine-17 of G-CSF.

11. Canceled.

~~12. The fusion protein of any one of Claims 1-5, wherein the soluble protein is growth hormone (GH).~~

13. Canceled.

~~14. The fusion protein of any one of Claims 1-5, wherein the soluble protein is selected from the group consisting of granulocyte-macrophage colony stimulating factor (GM-CSF), interleukin-11 (IL-11), thrombopoietin (TPO), stem cell factor (SCF) and flt3 ligand.~~

15. A homomultimeric fusion protein comprising two or more copies of a member of the Growth Hormone (GH) supergene family joined without an intervening peptide linker.

16. A homomultimeric fusion protein comprising two or more copies of a member of the Growth Hormone (GH) supergene family joined by at least one peptide linker, wherein the member of the GH supergene family is selected from the group consisting of: growth hormone, prolactin, placental lactogen, thrombopoietin (TPO), interleukin(IL)-2, interleukin-3, interleukin-4, interleukin-5, interleukin-6, interleukin-7, interleukin-9, interleukin-10, interleukin-11, interleukin-12 (p35 subunit), interleukin-13, interleukin-15, oncostatin M, ciliary neurotrophic factor, leukemia inhibitory factor, alpha interferon, beta interferon, gamma interferon, omega interferon, tau interferon, granulocyte-colony stimulating factor (G-

CSF), granulocyte-macrophage colony stimulating factor (GM-CSF), cardiotrophin-1, macrophage colony stimulating factor, Stem Cell Factor and flt-3 ligand.

sub 17 17. The homomultimeric fusion protein of any one of claims 15-16, wherein the member of the GH supergene family is granulocyte-colony stimulating factor (G-CSF).

18. The homomultimeric fusion protein of claim 17, wherein the homomultimeric fusion protein is a dimeric G-CSF fusion protein.

19. The homomultimeric fusion protein of Claim 15, wherein the member of the GH supergene family is EPO.

sub 20 20. The homomultimeric fusion protein of any one of Claims 19 or 40, wherein the multimeric fusion protein is a dimeric EPO fusion protein.

21. The homomultimeric fusion protein of any one of claims 15-16, wherein the member of the GH supergene family is selected from the group consisting of: growth hormone, alpha interferon, beta interferon, gamma interferon, GM-CSF, IL-11, TPO, SCF, and Flt3 ligand.

22. The fusion protein of any one of claims 15, 16, 40 or 41, wherein the peptide linker is SerGly.

23. The fusion protein of any one of claims 15, 16, 40 or 41, wherein the peptide linker is Ser(GlyGlySer)_n, wherein n is 1 to 7.

24. A purified fusion protein according to any one of Claims 1 or 2, wherein the purified fusion protein is dimeric and is essentially free of monomeric fusion protein.

25. The purified fusion protein of claim 24, wherein the soluble protein is selected from the group consisting of G-CSF, EPO and interleukin-11.

26. A method of producing a fusion protein according to any one of Claims 1, 2, 15, 16, 20 or 41, comprising:

- a. transfecting or transforming a host cell with at least one nucleic acid encoding an immunoglobulin domain and a soluble protein selected from the group consisting of a growth factor, a cytokine, and an active variant thereof;
- b. culturing the host cell; and
- c. harvesting the fusion protein expressed by the host cell.

27. The method of claim 26, wherein the nucleic acid further encodes a peptide linker.

sub 28 28. A nucleic acid encoding the fusion protein of any one of Claims 1, 2, 15, 16, 40 or 41.

29. A host cell transfected or transformed with the nucleic acid of claim 28, enabling the host cell to express the fusion protein.

30. The host cell of claim 29, wherein the host cell is a eukaryotic cell.

31. The host cell of claim 30, wherein the eukaryotic cell is a mammalian cell.

sub 32 32. A method of purifying the fusion protein according to any one of Claims 1, 2, 15, 16, 40 or 41, comprising:

- a. obtaining a composition comprising the fusion protein; and
- b. isolating the fusion protein from contaminants by column chromatography.

